REMARKS

On April 8, 1997, U.S. Patent No. 5,618,699 (hereinafter, the "'699 Patent") issued to Hiroshi Hamamoto, Yoshinori Sugiyama, Noriaki Nakagawa, Eiji Hashida, Suguru Tsuchimoto, Noriyuki Nakanishi, Yuji Matsunaga and Yoshimi Okada. The patent is entitled PLANT VIRUS VECTOR, PLASMID, PROCESS FOR EXPRESSION OF FOREIGN GENE AND PROCESS FOR OBTAINING FOREIGN GENE PRODUCT and claims a plant virus vector capable of systemically expressing a coat protein fusion protein in a plant. In addition, the patent claims a process for systemically expressing a fusion protein in a plant using the virus vector, a process for producing a fusion protein in a plant using the virus vector, and a virion particle comprising a coat protein of a Tobamovirus and a fusion protein. A copy of this patent is attached as Exhibit A for the Examiner's convenience.

Claims 14-17 have been added to the subject application. These claims define the same patentable invention as the claims of U.S. Patent No. 5,618,699.

Applicants' claims are supported in a number of different passages in the subject application. Only representative passages are cited below. Additional passages could have been listed, but have not been included for the sake of brevity.

PATENT CLAIM 1 AND APPLICANT'S CLAIM 14

Patent claim 1 is directed to a plant virus vector capable of expressing a foreign protein in a plant. The foreign protein is expressed as a fusion protein with the coat protein of the virus.

Applicants' claim 14 corresponds to patent claim 1 and is copied verbatim from the patent. Claim 14 is supported in Applicants' specification as follows:

Patent Claim 1

Applicants' Disclosure

1. A plant virus vector comprising

The present invention relates to the field of genetically engineered peptide



production in plants, more specifically, the invention relates to the use of tobamovirus vectors to express fusion proteins.

(Page 1, lines 8-11)

The subject invention provides novel recombinant plant viruses that code for the expression of fusion proteins that consist of a fusion between a plant viral coat protein and a protein of interest. (Page 4, lines 34-37)

In a preferred embodiment of the invention, the 17.5 Kda coat protein of tobacco mosaic virus is used in conjunction with a tobacco mosaic virus derived vector.

(Page 5, lines 14-17)

The TMVCP fusion vectors described in the following examples are based on the U1 or wild type TMV strain and are therefore compared to the parental virus as a control. (Page 14, lines 8-10)

Detailed information on how to make and use recombinant RNA plant viruses can be found, among other places in U.S. patent 5,316,931 (Donson et al.), which is herein incorporated by reference. (Page 10, lines 14-17; Column 10, lines 1-11 of U.S. Patent No. 5,316,931 states: "Initiation of TMV assembly occurs by intereaction between ring-shaped aggregates ("discs") of coat protein (each disc consisting of two layers of 17 subunits) and a unique internal nucleation site in the RNA; a hairpin region about 900 nucleotides from the 3' end in the common strain of TMV. Any RNA, including subgenomic RNAs containing this site, may be packaged into virions. The discs apparently assume a helical form on interaction with the RNA, and assembly (elongation) then proceeds in both directions (but much more rapidly in the 3'- to 5'-direction from the nucleation site).

a viral assembly origin



The expression of the subject coat fusion proteins may be driven by any of a variety of promoters functional in the genome of the recombinant plant viral vector. In a preferred embodiment of the invention, the subject fusion protein are expressed from plant viral subgenomic promoters using vectors as described in U.S. Patent 5,316,931. (Page 9, lines 27-32)

As tobamovirus coat proteins may self-assemble into virus particles, the virus particles of the invention may be assembled either <u>in vivo</u> or <u>in vitro</u>. (Page 10, lines 32-34)

The protein of interest portion of the fusion protein for expression may consist of a peptide of virtually any amino acid sequence...
(Page 5, lines 17-19)

The protein of interest portion of the subject fusion proteins may vary in size from one amino acid residue to over several hundred amino acid residues... (Page 6, lines 3-5)

The fusion proteins of the invention comprise two portions: (i) a plant viral coat protein and (ii) a protein of interest. (Page 5, lines 5-7)

In a preferred embodiment of the invention, the 17.5 Kda coat protein of tobacco mosaic virus is used in conjunction with a tobacco mosaic virus derived vector.
(Page 5, lines 14-17)

The fusion joint may be located at the amino terminus of the coat protein portion of the fusion protein (joined to the carboxyl terminus of the protein of interest).

(Page 6, lines 35-37)

Polynucleotide sequences encoding the

and a foreign protein gene

linked downstream of a coat protein gene of a Tobamovirus

via a nucleotide sequence of a Tobamovirus

which causes readthrough,

such that upon expression of the vector in a plant, the coat protein and a fusion protein of the coat protein and the foreign protein are systemically produced in the plant.

subject fusion proteins may comprise a "leaky" stop codon at a fusion joint. The stop codon may be present a s the codon immediately adjacent to the fusion joint, or may be located close (e.g., within 9 bases) to the fusion joint. A leaky stop codon may be included in polynucleotides encoding the subject coat fusion protein so as to maintain a desired ratio of fusion protein to wild type coat protein. A "leaky" stop codon does not always result in translational termination and is periodically translated. (Page 8, lines 13-22)

Thus, by including a leaky stop codon at a fusion joint coding region in a recombinant viral vector encoding a coat fusion protein, the vector may be used to produce both a fusion protein and a second smaller protein, e.g., the viral coat protein.

(Page 8, lines 33-37)

In another embodiment of the virus particles of the invention, the virus particle coat may consist of a mixture of coat fusion proteins and non-fusion coat protein, wherein the ratio of the two proteins may be varied.

(Page 10, lines 28-32)

PATENT CLAIM 9 AND APPLICANTS' CLAIM 15

Patent claim 9 is directed to a process for systemically expressing a fusion protein of a coat protein and a foreign protein in a plant.

Applicants' new claim 15 corresponds to patent claim 9 and is copied verbatim from the '699 patent. Claim 15 is supported in Applicants' specification as follows:

Patent Claim 9

- 9. A process for systemically expressing a fusion protein of a coat protein and a foreign protein in a plant comprising the steps of:
- (a) inoculating a plant with a plant virus vector,

Applicants' Disclosure

The recombinant plant viruses of the invention provide for systemic expression of the fusion protein, by systemically infecting cells in a plant. (Page 4, line 37 to page 5, line 2)

The invention also provides for recombinant plant cells comprising the



subject coat fusion proteins and/or virus particles comprising the subject coat fusion proteins. These plant cells may be produced either by infecting plant cells (either in culture or in whole plants) with infections virus particles of the invention or with polynucleotides encoding the genomes of the infectious virus particles of the invention.

(Page 11, lines 1-7)

The present invention relates to the field of genetically engineered peptide production in plants, more specifically, the invention relates to the use of tobamovirus vectors to express fusion proteins.

(Page 1, lines 8-11)

The subject invention provides novel recombinant plant viruses that code for the expression of fusion proteins that consist of a fusion between a plant viral coat protein and a protein of interest. (Page 4, lines 34-37)

In a preferred embodiment of the invention, the 17.5 Kda coat protein of tobacco mosaic virus is used in conjunction with a tobacco mosaic virus derived vector. (Page 5, lines 14-17)

The TMVCP fusion vectors described in the following examples are based on the U1 or wild type TMV strain and are therefore compared to the parental virus as a control. (Page 14, lines 8-10)

Detailed information on how to make and use recombinant RNA plant viruses can be found, among other places in U.S. patent 5,316,931 (Donson et al.), which is herein incorporated by reference. (Page 10, lines 14-17; Column 10, lines 1-11 of U.S. Patent No. 5,316,931 states: "Initiation of TMV assembly occurs by intereaction between ring-shaped aggregates ("discs") of coat protein (each

wherein the plant virus vector comprises

a viral assembly origin



disc consisting of two layers of 17 subunits) and a unique internal nucleation site in the RNA; a hairpin region about 900 nucleotides from the 3' end in the common strain of TMV. Any RNA, including subgenomic RNAs containing this site, may be packaged into virions. The discs apparently assume a helical form on interaction with the RNA, and assembly (elongation) then proceeds in both directions (but much more rapidly in the 3'- to 5'-direction from the nucleation site).

The expression of the subject coat fusion proteins may be driven by an y of a variety of promoters functional in the genome of the recombinant plant viral vector. In a preferred embodiment of the invention, the subject fusion protein are expressed from plant viral subgenomic promoters using vectors as described in U.S. Patent 5,316,931. (Page 9, lines 27-32)

As tobamovirus coat proteins may self-assemble into virus particles, the virus particles of the invention may be assembled either <u>in vivo</u> or <u>in vitro</u>. (Page 10, lines 32-34)

The protein of interest portion of the fusion protein for expression may consist of a peptide of virtually any amino acid sequence...
(Page 5, lines 17-19)

The protein of interest portion of the subject fusion proteins may vary in size from one amino acid residue to over several hundred amino acid residues... (Page 6, lines 3-5)

The fusion proteins of the invention comprise two portions: (i) a plant viral coat protein and (ii) a protein of interest. (Page 5, lines 5-7)

In a preferred embodiment of the invention, the 17.5 Kda coat protein of

and a foreign protein gene

linked downstream of a coat protein gene of a Tobamovirus





tobacco mosaic virus is used in conjunction with a tobacco mosaic virus derived vector. (Page 5, lines 14-17)

The fusion joint may be located at the amino terminus of the coat protein portion of the fusion protein (joined to the carboxyl terminus of the protein of interest).

(Page 6, lines 35-37)

via a nucleotide sequence of a Tobamovirus which causes readthrough,

such that upon expression of the vector in a plant, the coat protein and the fusion protein are systemically produced in the plant; and

Polynucleotide sequences encoding the subject fusion proteins may comprise a "leaky" stop codon at a fusion joint. The stop codon may be present a s the codon immediately adjacent to the fusion joint, or may be located close (e.g., within 9 bases) to the fusion joint. A leaky stop codon may be included in polynucleotides encoding the subject coat fusion protein so as to maintain a desired ratio of fusion protein to wild type coat protein. A "leaky" stop codon does not always result in translational termination and is periodically translated. (Page 8, lines 13-22)

Thus, by including a leaky stop codon at a fusion joint coding region in a recombinant viral vector encoding a coat fusion protein, the vector may be used to produce both a fusion protein and a second smaller protein, e.g., the viral coat protein.

(Page 8, lines 33-37)

In another embodiment of the virus particles of the invention, the virus particle coat may consist of a mixture of coat fusion proteins and non-fusion coat protein, wherein the ratio of the two proteins may be varied. (Page 10, lines 28-32)



(b) expressing the fusion protein systemically in the plant.

The recombinant plant viruses of the invention provide for systemic expression of the fusion protein, by systemically infecting cells in a plant. (Page 4, line 37 to page 5, line 2)

PATENT CLAIM 13 AND APPLICANTS' CLAIM 16

Patent claim 13 is directed to a process for producing a fusion protein of a coat protein and a foreign protein in a plant.

Applicants' new claim 16 corresponds to patent claim 13 and is copied verbatim from the patent. Claim 13 is supported in Applicants' specification as follows.

Patent Claim 13

A process for producing a fusion protein of a coat protein and a foreign protein in a plant comprising the steps of:

(1) inoculating a plant with a plant virus vector,

wherein the plant virus vector comprises

Applicants' Disclosure

Thus by employing the recombinant plant viruses of the invention, large quantities of a protein of interest may be produced.

(Page 5, lines 2-4)

The invention also provides for recombinant plant cells comprising the subject coat fusion proteins and/or virus particles comprising the subject coat fusion proteins. These plant cells may be produced either by infecting plant cells (either in culture or in whole plants) with infections virus particles of the invention or with polynucleotides encoding the genomes of the infectious virus particles of the invention.

(Page 11, lines 1-7)

The present invention relates to the field of genetically engineered peptide production in plants, more specifically, the invention relates to the use of tobamovirus vectors to express fusion proteins.

(Page 1, lines 8-11)

The subject invention provides novel recombinant plant viruses that code for the expression of fusion proteins that



consist of a fusion between a plant viral coat protein and a protein of interest. (Page 4, lines 34-37)

In a preferred embodiment of the invention, the 17.5 Kda coat protein of tobacco mosaic virus is used in conjunction with a tobacco mosaic virus derived vector.

(Page 5, lines 14-17)

The TMVCP fusion vectors described in the following examples are based on the U1 or wild type TMV strain and are therefore compared to the parental virus as a control. (Page 14, lines 8-10)

Detailed information on how to make and use recombinant RNA plant viruses can be found, among other places in U.S. patent 5,316,931 (Donson et al.), which is herein incorporated by reference. (Page 10, lines 14-17; Column 10, lines 1-11 of U.S. Patent No. 5,316,931 states: "Initiation of TMV assembly occurs by intereaction between ring-shaped aggregates ("discs") of coat protein (each disc consisting of two layers of 17 subunits) and a unique internal nucleation site in the RNA; a hairpin region about 900 nucleotides from the 3' end in the common strain of TMV. Any RNA, including subgenomic RNAs containing this site, may be packaged into virions. The discs apparently assume a helical form on interaction with the RNA, and assembly (elongation) then proceeds in both directions (but much more rapidly in the 3'- to 5'-direction from the nucleation site).

The expression of the subject coat fusion proteins may be driven by an y of a variety of promoters functional in the genome of the recombinant plant viral vector. In a preferred embodiment of the invention, the subject fusion protein are expressed from plant viral subgenomic

a viral assembly origin





promoters using vectors as described in U.S. Patent 5,316,931. (Page 9, lines 27-32)

As tobamovirus coat proteins may self-assemble into virus particles, the virus particles of the invention may be assembled either <u>in vivo</u> or <u>in vitro</u>. (Page 10, lines 32-34)

The protein of interest portion of the fusion protein for expression may consist of a peptide of virtually any amino acid sequence...
(Page 5, lines 17-19)

The protein of interest portion of the subject fusion proteins may vary in size from one amino acid residue to over several hundred amino acid residues... (Page 6, lines 3-5)

The fusion proteins of the invention comprise two portions: (i) a plant viral coat protein and (ii) a protein of interest. (Page 5, lines 5-7)

In a preferred embodiment of the invention, the 17.5 Kda coat protein of tobacco mosaic virus is used in conjunction with a tobacco mosaic virus derived vector.

(Page 5, lines 14-17)

The fusion joint may be located at the amino terminus of the coat protein portion of the fusion protein (joined to the carboxyl terminus of the protein of interest). (Page 6, lines 35-37)

Polynucleotide sequences encoding the subject fusion proteins may comprise a "leaky" stop codon at a fusion joint. The stop codon may be present as the codon immediately adjacent to the fusion joint, or may be located close (e.g., within 9 bases) to the fusion joint. A leaky stop codon may be included in polynucleotides encoding the subject coat fusion protein so as to maintain a

and a foreign protein gene

linked downstream of a coat protein gene of a Tobamovirus

via a nucleotide sequence of a Tobamovirus which causes readthrough,





desired ratio of fusion protein to wild type coat protein. A "leaky" stop codon does not always result in translational termination and is periodically translated. (Page 8, lines 13-22)

such that upon expression of the vector in a plant, the coat protein and the fusion protein are systemically produced in the plant; Thus, by including a leaky stop codon at a fusion joint coding region in a recombinant viral vector encoding a coat fusion protein, the vector may be used to produce both a fusion protein and a second smaller protein, e.g., the viral coat protein.

(Page 8, lines 33-37)

In another embodiment of the virus particles of the invention, the virus particle coat may consist of a mixture of coat fusion proteins and non-fusion coat protein, wherein the ratio of the two proteins may be varied.

(Page 10, lines 28-32)

the coat protein and the fusion protein of the coat protein and the foreign protein are systemically produced in the plant;

The recombinant plant viruses of the invention provide for systemic expression of the fusion protein, by systemically infecting cells in a plant. (Page 4, line 37 to page 5, line 2)

Thus by including a leaky stop codon at a fusion joint coding region in a recombinant viral vector encoding a coat fusion protein, the vector may be used to produce both a fusion protein and a second smaller protein, e.g., the viral coat protein.

(Page 8, lines 33-37)

In another embodiment of the virus particles of the invention, the virus particle coat may consist of a mixture of coat fusion proteins and non-fusion coat protein, wherein the ratio of the two proteins may be varied.

(Page 10, lines 28-32)

(2) recovering virions from the plant; and

In addition to providing the described viral coat fusion proteins, the invention also provides for virus particles that comprise the subject fusion proteins.





(Page 10, lines 24-26)

(3) isolating the fusion protein from the virions.

The virus particles may also be conveniently disassembled using well known techniques so as to simplify the purification of the subject fusion proteins, or portions thereof. (Page 10, lines 34-37)

In another embodiment of the invention, the fusion joints on the subject coat fusion proteins are designed so as to comprise an amino acid sequence that is a substrate for protease. By providing a coat fusion protein having such a fusion joint, the protein of interest may be conveniently derived from the coat protein fusion by using a suitable proteolytic enzyme. (Page 9, lines 19-25)

PATENT CLAIM 16 AND APPLICANTS' CLAIM 17

Patent claim 16 is directed to a virion particle comprising a coat protein of a Tobamovirus and a fusion protein of the coat protein and a foreign protein.

Applicants' claim 17 corresponds to patent claim 16 and is copied verbatim from the patent. Claim 17 is supported in Applicants' specification as follows:

Patent Claim 16

16. A virion particle comprising a coat protein of a Tobamovirus and a fusion protein of the coat protein and a foreign protein.

Applicants' Disclosure

In addition to providing the described viral coat fusion proteins, the invention Also provides for virus particles that comprise the subject fusion proteins. The coat of the virus particles of the invention may consist entirely of coat fusion protein. In another embodiment of the virus particles of the invention, the virus particle coat may consist of a mixture of coat fusion proteins and nonfusion coat protein, wherein the ratio of the two proteins may be varied. (Page 10, lines 24-32)

PROPOSED COUNTS

The following four counts are proposed for purposes of interference:



PROPOSED COUNT 1

1. A plant virus vector comprising a viral assembly origin and a foreign protein gene linked downstream of a coat protein gene of a Tobamovirus via a nucleotide sequence of a Tobamovirus which causes readthrough, such that upon expression of the vector in a plant, the coat protein and a fusion protein of the coat protein and the foreign protein are systemically produced in the plant.

Proposed Count 1 corresponds exactly to patent claim 1. Claims 2-7 and claims 14-15 are dependent upon claim 1. Thus, claim 1 encompasses all of the subject matter of claims 2-7 and 14-15.

PROPOSED COUNT 2

- 2. A process for systemically expressing a fusion protein of a coat protein and a foreign protein in a plant comprising the steps of:
 - (a) inoculating a plant with a plant virus vector, wherein the plant virus vector comprises a viral assembly origin and a foreign protein gene linked downstream of a coat protein gene of a Tobamovirus via a nucleotide sequence of a Tobamovirus which causes readthrough, such that upon expression of the vector in the plant, the coat protein and the fusion protein are systemically produced in the plant; and
 - (b) expressing the fusion protein systemically in the plant.

Proposed Count 2 corresponds exactly to patent claim 9. Claims 10-12 are dependent upon claim 9. Thus, claim 9 encompasses all of the subject matter of claims 10-12.

PROPOSED COUNT 3

- 3. A process for producing a fusion protein of a coat protein and a foreign protein in a plant comprising the steps of:
 - (1) inoculating a plant with a plant virus vector, wherein the plant virus vector comprises a viral assembly origin and a foreign protein gene linked downstream of a coat protein gene of a Tobamovirus via a nucleotide sequence of a Tobamovirus which causes readthrough, such that upon expression of the vector in a plant, the coat protein and the fusion protein of the coat protein and the foreign protein are systemically produced in the plant;
 - (2) recovering virions from the plant; and
 - (3) isolating the fusion protein from the virions.

Proposed Count 3 corresponds exactly to patent claim 13.

PROPOSED COUNT 4

4. A virion particle comprising a coat protein of a Tobamovirus and a fusion protein of the coat protein and a foreign protein.

Proposed Count 4 corresponds exactly to patent claim 16.

The Remaining Independent Claims

The remaining independent claims in the '699 Patent are claims 17, 18, 22 and 24.

Patent claim 17 is not patentably distinct from patent claim 9 (Proposed Count 2), as the former merely recites the subspecies coat protein of a Tobamovirus, which is encompassed by claim 9.



Patent claim 18 is not patentable over the corresponding generic patent claim 1 (Proposed Count 1), as claim 18 merely recites the subspecies tobacco mosaic viral (TMV) vector and specific DNA readthrough sequences, which are encompassed by claim 1. Claims 19-21 depend from claim 18.

Patent claim 22 is not patentable over the corresponding generic patent claim 9 (Proposed Count 2), as claim 22 merely recites the subspecies TMV vector and TMV coat protein, which are encompassed by claim 9. Claim 23 depends from claim 22.

Patent claim 24 is not patentable over the corresponding generic patent claim 13 (Proposed Count 3), as claim 24 merely recites the subspecies TMV vector and TMV coat protein, which are encompassed by claim 13. Claim 25 depends from claim 24.

CLAIMS TO BE DESIGNATED AS CORRESPONDING TO THE COUNTS

As noted in 37 C.F.R. § 1.606, all claims that "define the same patentable invention as the count shall be designated as corresponding to the count" and "any single patent claim will be presumed…not to contain separate patentable inventions."

PROPOSED COUNT 1

Claims 2-8 and 14-15 depend from claim 1 in U.S. Patent No. 5,618,699.

Additionally, as explained above, claim 18 is not patentable over the corresponding generic claim 1 as it merely recites a subspecies of claim 1. Claims 19-21 depend from claim 18.

Thus, applying the provisions of 37 C.F.R. § 1.606 to these claims, claims 1-8, 14-15 and 18-21 in the '699 patent are directed to the same patentable invention. Accordingly, claims 1-8, 14-15 and 18 should be designated as corresponding to Proposed Count 1.

Applicants' new claim 14 should also be designated as corresponding to Proposed Count 1, as this claim defines the same patentable invention as patent claims 1-8, 14-15 and 18-21.



PROPOSED COUNT 2

Applicants' Proposed Count 2 is identical to claim 9 in U.S. Patent No. 5,618,699. Claims 10-12 depend from claim 9. Additionally, as explained above, claim 17 and claim 22 in the patent are not patentable over the corresponding generic claim 9, as each merely recites a subspecies coat protein and/or viral vector of claim 9. Claim 23 depends from claim 22. Thus, applying the provisions of 37 C.F.R. § 1.606 to these claims, claims 9-12, 17 and 22 are directed to the same patentable invention. Accordingly, claims 9-12, 17, 22 and 23 should be designated as corresponding to Proposed Count 2.

Applicants' new claim 15 should also be designated as corresponding to Proposed Count 2, as this claim defines the same patentable invention as patent claims 9-12, 17, 22 and 23.

PROPOSED COUNT 3

Applicants' Proposed Count 3 is identical to claim 13 in U.S. Patent No. 5,618,699. No other claims depend from claim 13. However, as explained above, claim 24 is not patentable over the corresponding generic claim 13 as it merely recites a subspecies TMV vector and coat protein of claim 13. Claim 25 depends from claim 24. Thus, applying the provisions of 37 C.F.R. § 1.606 to these claims, claims 13, 24 and 25 are directed to the same patentable invention. Accordingly, claims 13, 24 and 25 should be designated as corresponding to Proposed Count 3.

Applicants' new claim 16 should also be designated as corresponding to Proposed Count 3, as this claim defines the same patentable invention as patent claims 13, 24 and 25.

PROPOSED COUNT 4

Applicants' Proposed Count 4 corresponds to claim 16 of the '699 Patent. No other claims depend from claim 16. Accordingly, claim 16 of the '699 Patent should be designated as corresponding to Proposed Count 4.

Applicants' new claim 17 should also be designated as corresponding to Proposed Count 4, as this claim defines the same patentable invention as patent claim 16.



The designation of Applicants' claims 14-17 as corresponding to Proposed Counts 1-4, respectively, is not to be construed as Applicants' acquiescence in the correctness of the designation or the correctness of the Counts or a concession that each claim is directed to a single patentable invention. Applicants reserve the right to challenge to propriety of the Proposed Counts, the designation of any claim as corresponding to a particular Proposed Count, and the patentability of any claim during the preliminary motion period in an interference, or otherwise.

ENTITLEMENT TO EARLIER FILING DATE UNDER 35 U.S.C. § 120

Applicants have amended the specification to claim the benefit of earlier-filed related applications. An identical amendment was made to the parent U.S. Patent Application Serial No. 08/324,003, and was entered by the Examiner as indicated in the Office Action mailed December 8, 1997.

It should also be noted that in parent application 08/324,003, in the Office Action mailed February 27, 1997, the Examiner stated:

Applicants' effective filing date of **February 1989** has obviated the prior art rejections over Takamatsu *et al.*, WO 92/18618 and Hamamoto *et al.* (emphasis added)

The Hamamoto reference cited by the Examiner is Hamamoto, H., Sugiyama, Y., Nakagawa, N., Hashida, E., Matsunaga, Y., Takemoto, S., Watanabe, Y., and Okada, Y. 1993b, "A new tobacco mosaic virus vector and its use for the systemic production of angiotensin-I-converting enzyme inhibitor in transgenic tobacco and tomato," <u>Bio/Technology</u> 11:930-932 (1993).

COMPLIANCE WITH 37 C.F.R. § 1.607(a)

This request for interference complies with the requirements of 37 C.F.R. § 1.607(a):

- (1) The patent is identified as U.S. Patent No. 5,618,699 to Hamamoto et al.;
- (2) At least one proposed counts have been presented;
- (3) Claims in the '699 Patent corresponding to each Proposed Count:



- (a) Claims 1-8, 14-15 and 18-21 in the '699 Patent should be designated as corresponding to Proposed Count 1;
- (b) Claims 9-12, 17 and 22-23 in the '699 Patent should be designated as corresponding to Proposed Count 2;
- (c) Claims 13, 24 and 25 in the '699 Patent should be designated as corresponding to Proposed Count 3;
- (d) Claim 16 in the '699 Patent should be designated as corresponding to Proposed Count 4;
- (4) Applicants' claims corresponding to each Proposed Count:
 - (a) Applicants' claim 14 should be designated as corresponding to Proposed Count 1;
 - (b) Applicants' claim 15 should be designated as corresponding to Proposed Count 2;
 - (c) Applicants' claim 16 should be designated as corresponding to Proposed Count 3;
 - (d) Applicants' claim 17 should be designated as corresponding to Proposed Count 4;
- (5) Applicants' claims 14-17 have been applied to the subject application.

Applicants respectfully request that an interference be expeditiously declared with U.S. Patent 5,618,699. Applicants further request that they be accorded benefit of the filing date of October 14, 1994.

A showing under 37 C.F.R. § 1.608(b) is not required, because Applicants' effective filing date of October 14, 1994 antedates the date of November 30, 1994, which is the earliest date that could possibly be accorded to Hamamoto et al. Applicant does not concede that Hamamoto et al. are entitled to the filing date of November 30, 1994.

The Commissioner is hereby authorized to charge any fee or underpayment, or credit any overpayment, to the Howrey & Simon Deposit Account No. 08-3038 for any matter in



Dated: April 7, 1998

connection with this communication, including any fee for extension of time which may be required.

Respectfully submitted,

Albert P. Halluin

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